APR 2 3 1996

DP Barcodes: D221657, D222036 and D224393 Case: 046566

MEMORANDUM

Subject: EPA File Symbol/EPA Reg. No.: 241-GTT/**FOR USE IN IMI-CORN™ ONLY; AC 513,996**

From: Carol E. Glasgow, Ph.D., Toxicologist
Precautionary Review Section
Registration Support Branch (7505W)
Registration Division (7505C)

To: Robert Taylor, PM 25
Fungicide-Herbicide Branch
Registration Division (7505C)

Applicant: American Cyanamid Company
P.O. Box 400
Princeton, NJ 08543-0400

FORMULATION FROM LABEL:

Active Ingredient (s):	% by weight
Imazethapyr (±)-2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1H-imidazol-2-yl]-5-ethyl-3-pyridinecarboxylic acid	52.5
Imazapyr 2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1H-imidazol-2-yl]-3-pyridinecarboxylic acid)	17.5
Inert ingredient(s)	30.0

BACKGROUND: American Cyanamid Company submitted a primary eye irritation study to support registration of its new product referenced above. Study performed by American Cyanamid Company Agricultural Research Division on MRID 438615-13. This product was discussed at the PRS Team meeting on April 1, 1996 as a candidate for bridging. The conclusion was that PRS could bridge the worst-case from most endpoints, but should review the primary eye irritation study for accuracy.

RECOMMENDATION: RSB/PRS findings are as follows:

The primary eye irritation study is **Acceptable**. However, PRS would appreciate more specific information about the acclimation period. The report specifies: "The animals were acclimated to laboratory conditions for at least 3 days after receipt." Review of the dates provided in the report shows the rabbits were received on January 19, 1995, and "experimental period began on January 30, 1995." Unless the rabbits were kept elsewhere for a portion of the time, the period of acclimation was 11 days. EPA prefers 5 days of acclimation; a shorter time

may be enough to reject the study if everything else is not perfect.

HED data provided the worst-case information on the two active ingredients for this product and the worst case situation is listed below.

TOXICITY PROFILES

Acute oral toxicity	IV	Acceptable
Acute dermal toxicity	III	Acceptable
Acute inhalation toxicity	III	Acceptable
Primary eye irritation	II	Acceptable
Primary dermal irritation	IV	Acceptable
Dermal sensitization	No	Acceptable

LABELING: The signal word for this product is "Warning" as the primary eye irritation study is category II. Language required for the label should include the following:

> Harmful if absorbed through skin, causes moderate eye injury. Avoid contact with skin, eyes or clothing. Wash thoroughly with soap and water after handling.

Statements of practical treatment language should include the following:

> *If on skin*: Wash with plenty of soap and water. Get medical attention.
> *If in eyes*: Flush eyes with plenty of water. Call a physician if irritation persists.

DATA EVALUATION REVIEW FOR PRIMARY EYE IRRITATION (§81-4)

Product Manager: 25 **Reviewer**: Carol Glasgow, Ph.D.
MRID No.: 438615-13 **Report Date**: September 1, 1995
Testing Laboratory: American Cyanamid Company, Agricultural Research Division
Report No.: T-0792
Author(s): Lisa M. Boczon
Species: New Zealand White albino rabbit
Weight: not given
Age: 10 - 13 weeks
Sex: 6 males
Source: Skipjack farms, Skipjack, Pennsylvania
Test Material: AC 263,499/AC 243,997 70 DG Formulation, Lot Number AC 9786-68B; tan granules
Quality Assurance (40 CFR §160.12): Included, acceptable

Summary:

1. **Toxicity Category**: II

2. **Classification**: Acceptable

Procedure (Deviation from §81.4): Animals acclimated to laboratory conditions a minimum of 3 days before testing. Animals' eyes examined two ways before treatment: 1) macroscopically with hand-held light source, and 2), with fluorescein and a UV light source. Animals with preexisting eye damage not used in study. Test substance ground into powder and 100 mg instilled into the conjunctival sac of the left eye. Contralateral eye used for control. Eyelids held shut for about 1 second to keep maximum contact. Eyes examined approximately 1 hour after treatment, at 24, 48, and 72 hours, and at days 4, 7, 10, 14, 17 and day 21. After first examination, fluorescein and the UV light source used for corneal examinations until no effect noted. Draize eye scale used for grading ocular irritation. Unusual ocular observations noted below.

Results: This product is a severe eye irritant, causing corneal damage and conjunctival irritation in all animals for up to 3 days. Corneal grade 2 in 2 animals. Corneas of all animals clear by day 21. Two rabbits exhibited corneal vascularization beginning at day 7. Iritis seen in 5/6 rabbits, but cleared in all animals within 72 hours. Conjunctivitis reaching grade 3 for redness in 3 rabbits as early as 24 hours. Chemosis and discharge were less severely affected, with up to grade 2 in 4/6 animals. Conjunctival irritation cleared by day 14 in all test subjects.

3